

CLAIMS

1. A method of assay comprising subjecting a sample to a quantitative or qualitative determination of the presence in the sample of (a) an auto-reactive immune system component specifically recognising an epitope containing an isomerised peptide linkage and/or an optically inverted amino acid, and/or (b) an auto-antigen or a fragment thereof containing a said epitope and/or (c) a non-self antigen or fragment thereof which contains a said epitope and is capable of inducing an autoimmune response.
2. A method as claimed in Claim 1, wherein said immune system component is a cellular immune system component.
3. A method as claimed in Claim 2, wherein said immune system component is a T-lymphocyte.
4. A method as claimed in Claim 1, wherein said immune system component is a humoral immune system component.
5. A method as claimed in Claim 4, wherein said epitope comprises an amino acid sequence derived from IgG containing an isomerised peptide linkage or optically inverted amino acid.
6. A method as claimed in Claim 4, wherein said immune system component is an auto-antibody directed against an epitope comprising the amino acid *Asx contained in any one of the sequences:

Trp-Leu-*Asx-Gly-Lys-Glu-Tyr

Trp-Glu-Ser-*Asx-Gly

His-Phe-Phe-Lys-*Asx-Ile-Val-Thr-Pro

Pro-Ser-*Asx-Glu-Gly-Lys-Gly-Arg

5 Ala-Leu-Gly-Ile-Gly-Thr-*Asx-Ser-Val-Ile

Trp-Ser-Phe-Gly-Ser-Glu-*Asx-Gly-Ser-Gly-*Asx-Ser-Glu-
Asn

Ala-Gly-Trp-Leu-*Asx-Gly-Ser-Val-Arg

Gly-Arg-Val-Arg-Val-*Asx-Ser-Ala-Tyr.

10 where Asx* is α D Asp or Asn, or is β L or β D, Asp formed
by isomerisation/optical inversion of Asp or Asn residues
in the original sequence.

7. A method as claimed in Claim 4, wherein said immune system
15 component is an auto-antibody directed against an epitope
comprising the amino acid *Asx contained either of the
sequences:

Met-Glu-Val-Gly-Trp-Tyr-Arg-Pro-Pro-Phe-Ser-Arg-Val-Val-
His-Leu-Tyr-Arg-*Asx-Gly-Lys- or

20 Val-Val-His-Phe-Phe-Lys-*Asx-Ile-Val-Thr-Pro

where *Asx is α D Asp or Asn, or is β D, or β L Asp formed by
isomerisation/optical inversion of Asp or Asn residues in
the original sequence.

25 8. A method as claimed in Claim 4, wherein said immune system
component is an auto-antibody directed against an epitope
comprising the amino acid *Glx contained in any one of the
sequences:

Pro-Ser-*Glx-Gly-Lys-Gly-Arg

30 Phe-Ser-Trp-Gly-Ala-*Glx-Gly-Arg or

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Asp-Ala-*Glx-Gly-Thr-Leu-Ser-Lys

where *Glx is α D Glu or Gln, or is γ L or γ D Glu formed by isomerisation/optical inversion of Glu or Gln residues in the original sequence.

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9. A method as claimed in any one Claims 1 to 8, wherein detection of said immune system component or auto-antigen is indicative of an auto-immune disease.

10 10. A method as claimed in Claim 9, wherein said disease is rheumatoid arthritis, multiple sclerosis, insulin dependent diabetes mellitus, myasthenia gravis, celiac disease, Chagas' disease, psoriasis, or Crohn's disease.

15 11. A method for the detection of an auto-antigen or fragment thereof comprising detecting the reactivity of said auto-antigen or fragment with an immunological binding partner specific for the presence in said auto-antigen of an isomerised peptide linkage or an optically inverted amino
20 acid.

12. A method as claimed in Claim 11, wherein said immunological binding partner is specific for an epitope as defined in any one of Claims 6 to 8.

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13. A method as claimed in any preceding claim, providing information as to the amount of said immune system component or auto-antigen or non-self antigen or antigen fragment detected.

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14. A method for locating an epitope or epitopes in an auto-antigen comprising using L-iso-aspartyl (D-aspartyl) methyl-transferase (IAMT) and a source of labelled methyl groups to introduce said labelled methyl groups at one or more isomerised peptide linkage and/or optically inverted amino acids in said auto-antigen, and determining at least one location in said auto-antigen at which said labelled methyl groups are thus introduced, establishing the amino acid sequence of said auto-antigen in a region encompassing a said location and testing a peptide of said amino acid sequence incorporating at said location said isomerised or optically inverted amino acid for immuno-reactivity with an auto-reactive immune system component.
15. A method as claimed in Claim 14, wherein the auto-antibodies are associated with an autoimmune disease.
16. A method as claimed in Claim 14, wherein the autoimmune disease is rheumatoid arthritis, multiple sclerosis, insulin dependent diabetes mellitus, myasthenia gravis, celiac disease, Chagas' disease, psoriasis, or Crohn's disease.
17. A peptide containing an epitope recognised by an auto-reactive immune system component, which epitope contains an isomerised peptide linkage and/or an optically inverted amino acid.
18. A peptide as claimed in Claim 17, containing an epitope as defined in any one of Claims 6 to 8.

19. A peptide as claimed in Claim 18, comprising the altered amino acid residue *Asx, or *Glx and at least 3 flanking amino acid residues in the N-terminal and/or C-terminal direction, where *Glx is α D Glu or Gln, or is γ L or γ D Glu formed by isomerisation/optical inversion of Glu or Gln residues in the original sequence and where *Asx is α D Asp or Asn, or is β L or β D Asp formed by isomerisation/optical inversion of Asn or Asp residues in the original sequence.

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